Claims 2, 4-6, 11-12, 15-16, 21, and 24 have been amended. Claims 3 and 25-27 have been cancelled without prejudice or disclaimer of Applicants' right to pursue the subject matter of the cancelled claims in this or a subsequent application. New claims 28-31 have been added. Support for the amendments may be found throughout the specification. Support for the amendments to claim 2 can be found in claim 3 as originally filed. Support for the amendments to claims 5 and 6 can be found page 27, line 17 to page 28, line 19. Support for the amendments to claims 15-16 can be found at page 16, lines 18-23. Support for the amendments to claim 21 and new claim 31 can be found at page 18, line 17 to page 19, line 2. Support for new claims 28-30 can be found in original claims 11, 12 and 24. No new matter has been added by the amendments to the specification or the claims.

Claims 25-27 were rejected under 35 U.S.C. §101 because the claimed inventions recite a use without setting forth any steps involved in the process.

Although Applicants respectfully disagree, claims 25-27 have been cancelled without prejudice or disclaimer by the instant amendment. Thus the rejection is now moot.

Claim 21 was rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection is respectfully traversed.

Claim 21, as amended, distinctly claims the subject matter of the invention. As amended, claim 21 provides methods of screening for novel active compounds or compositions comprising a ginsenoside Rb_1 for the prevention, treatment, or therapy of diseases of the nervous tissues or spinal cord.

Claims 11, 12, and 24 were objected to under 37 CFR 1.75(c) as being in improper multiple dependent claim format.

The objection is traversed.

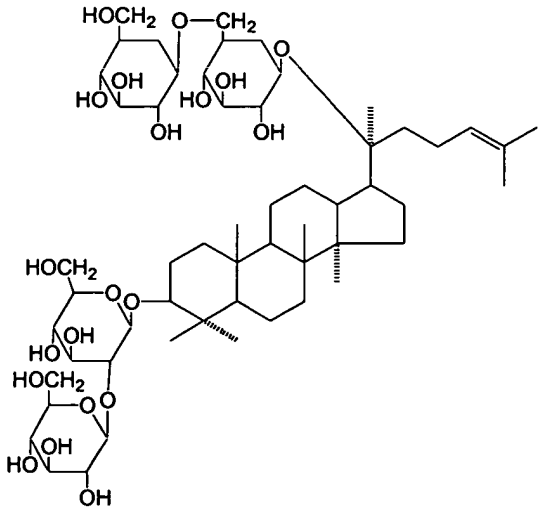
Claims 11, 12 and 24 have been amended and new claims 28-30 have been added which obviate the objection of original claims 11, 12, and 24.

Claims 1-24 were rejected under 35 U.S.C. §103(a), as being unpatentable over Lim et al. (Neuroscience Research 28, 191-200 (1997)) in view of Liu (U.S. Patent 4,708,949).

The rejection is respectfully traversed.

The present invention provides pharmaceutical compositions comprising ginsenoside Rb1, its metabolites, or salts thereof which are suitable for the prevention, treatment or therapy of diseases caused by injuries to the nervous tissues or to the spinal cord. The present invention further provides methods of screening for compounds or compositions which comprise ginsenoside Rb1 or a metabolite thereof, that are suitable for the prevention, treatment or therapy of diseases of the nervous tissue or the spinal cord.

As provided at page 6 of the specification, Ginsenoside Rb1 is a compound of the formula:



Applicant's respectfully submit that the present invention would not have been obvious to one skilled in the art from any combination of Lim and Liu at the time the invention was made. Moreover, it appears that the combination of Lim and Liu may not be proper.

As the reference is understood, Lim merely teaches intraperitoneal administration of ginsenoside Rb_1 to gerbils. More particularly, it appears the Lim teaches administering ginsenoside RB1 to gerbils can inhibit the occurrence of mild brain ischemia reperfusion injury (page 195, right column, lines 12 - 15). Moreover, **Lim teaches that Ginsenoside Rb1 can exhibit both neuroprotective and neurotoxic effects in gerbils under the administration conditions of the study** (page 197, right column, lines 14-18). Thus, the Lim publication would not have suggested to one skilled in the art at the time the invention was made that pharmaceutical compositions of ginsenoside Rb_1 would possess desirable properties for the prevention, treatment, or therapy of more serious nerve injury such as injuries to the head or spinal cord.

As the reference is understood, Liu teaches pharmaceutical compositions that are effective against cerebrovascular disease in which the active ingredient is a mixture of four plant extracts. Liu neither teaches nor suggests pharmaceutical compositions having ginsenoside Rb1 as the active ingredient. Moreover, the disclosure of Liu fails to teach mixtures comprising ginsenoside Rb1 as a component. The mixture of plant extracts taught by Liu appears to include ginsenoside but Liu neither discloses nor suggests any composition comprising ginsenoside Rb1.

One skilled in the art would not have been motivated to combine the teachings of Lim and Liu at the time that the instant invention was developed. More particularly, one skilled in the art would not have been motivated to replace the active ingredient, e.g., the multi-component plant extract mixture, of the pharmaceutical composition taught by Liu with ginsenoside Rb1 taught by Lim, in the methods of treating cerebrovascular disease taught by Lim.

Even if the disclosures of Lim and Liu are combined, the present invention still would not have been obvious to one skilled in the art based on any combination of the cited documents.

As the reference is understood, Lim neither discloses nor suggests that ginsenoside Rb_1 is capable of promoting regeneration and/or reconstruction of cerebral blood vessels, protecting oligodendrocytes, posessing antidemyelinating properties and suppressing secondary degeneration of nerve tissue. Applicants respectfully submit that one skilled in the art would not have reasonably inferred from Lim and/or Liu that ginsenoside Rb_1 or pharmaceutical compositions comprising same would possess any of the properties taught by the present invention.

Further, one skilled in the art would not have been motivated to prepare a pharmaceutical composition comprising ginsenoside Rb1 for the prevention, treatment or therapy of diseases caused by injuries to the nervous tissue or spinal cord based upon the results presented in Lim. More particularly, Lim teaches that ginsenoside Rb1 does not exhibit any therapeutic benefit to gerbils suffering from very minor injuries to the hippocampal CA1 region in transient forebrain ischemia model (page 195, left column, line 4 from the bottom - right column, line 15). Lim further teaches that high doses of ginsenoside Rb1, e.g., as high as 20 mg/kg in human patients, would be necessary to result in an operable pharmaceutical product comprising ginsenoside Rb1, which is impractical due to the availability of the bulk drug, raw material cost and risk of adverse side effects. Thus, as a matter of course, the person skilled in the art can not arrive at the idea to try to prepare a novel compound for treatment of brain and nerve diseases by utilizing ginsenoside Rb_1, as a lead compound by referring to said reference.

The disclosure of Liu is unable to overcome the limitations of the Lim reference.

As the reference is understood, Liu discloses a mixture of four plant extracts: ginsenoside (from ginsing), tetramethyl pyrazine (from Ligusticum), astragalan, and atractylol. Moreover, Liu teaches that the composition is effective in treating cerebrovascular disease and that the active ingredient of the recited pharmaceutical composition is formed form the specific combination of plant extracts. Thus, there is neither disclosure nor suggestion that compositions

containing other compounds, such as ginsenoside Rb1, would be effective against cerebrovascular diseases.

Moreover, Liu fails to disclose or suggest that any of the compositions disclosed therein would be effective in the treatment of nerve injury, particularly head injuries and/or spinal cord injuries. Liu also fails to disclose or suggest the use of any composition for use in promoting regeneration and reconstruction of cerebral blood vessels, protecting oligodendrocytes, antidemyelinating activity, or suppressing secondary degeneration of nerve tissue.

Liu merely teaches a mixture of four plant extracts and the effectiveness of this mixture against certain cerebrovascular diseases. Liu neither discloses nor suggests pharmaceutical compositions of ginsenoside Rb1 or that ginsenoside Rb1 possesses beneficial therapeutic properties for the prevention, treatment, or therapy of brain and nerve diseases. Thus, one skilled in the art one skilled in the art would not have been motivated based on Liu to prepare pharmaceutical compositions utilizing ginsenoside Rb1 as the pharmaceutically active component.

Neither Lim nor Liu considered alone or in combination teach or suggest methods of identifying pharmaceutical compositions which comprises ginsenoside Rb1 as the active ingredient. Thus, the screening methods provided by claims 21 - 23 of the present invention would not have been obvious in view of any combination of Lim and/or Liu.

In view thereof, reconsideration and withdrawal of the §103 rejection are requested.

Although it is not believed that any additional fees are needed to consider this submission, the Examiner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES TO CLAIMS

Please note that additions to the claims are shown underlined and deletions are shown in brackets.

IN THE CLAIMS:

Kindly cancel claims 3, 14, and 25-27 without prejudice or disclaimer.

Kindly amend claims 2, 4-6, 11-12, 15-16, 21, and 24, as follows:

2. (Amended) The pharmaceutical composition for prevention, treatment or therapy according to claim 1, comprising suppressing the secondary degeneration of the nervous tissues caused by injuries to the nervous tissues or to the spinal cord.

4. (Amended) The pharmaceutical composition for prevention, treatment or therapy according to claim 2 [or 3] wherein disease causing the secondary degeneration of the nervous tissues is spinal cord injury.

5. (Amended) The pharmaceutical composition for prevention, treatment or therapy according to claim 1 wherein said prevention, treatment or therapy is achieved by [means of vascular regeneration and/or reconstruction of the injured nervous tissues or spinal cord]ameliorating paralysis or paraplegia.

6. (Amended) The pharmaceutical composition for prevention, treatment or therapy according to claim 5 wherein disease [the blood vessels are cerebral blood vessels]causing the paralysis or paraplegia is spinal cord injury.

11. (amended) The pharmaceutical composition for prevention, treatment or therapy according to any one of claims 1 – [10]9 wherein the pharmaceutical composition is suitable [comprising the preparations]for intravenous administration.

12. (amended) The pharmaceutical composition for prevention, treatment or therapy according to any one of claims 1 – [10]9 wherein the pharmaceutical composition is suitable [comprising the preparations]for a single intravenous infusion or [the preparations]for continuous intravenous administration.

15. (amended) A pharmaceutical composition comprising ginsenoside Rb_1, its metabolites or salt thereof for prevention, treatment or therapy of trauma or [of deterioration of]traumatic injuries[to the nervous tissues or to the spinal cord or for treatment or therapy of traumatic injuries to the nervous tissues or to the spinal cord].

16. (amended) The pharmaceutical composition according to claim 15 wherein the trauma or traumatic injuries is or are spinal cord injuries, neurotrauma, or head injuries.

21. (amended) A method for [exploring]screening novel active compounds or compositions for prevention, treatment or therapy of diseases of the nervous tissues or the spinal cord comprising using ginsenoside Rb1 or its metabolites as a leading compound(s).

24. Pharmaceutical compositions for prevention, treatment or therapy of diseases of the nervous tissues or the spinal cord as obtained by the method according to claim 21 [- 23]or 22.

Kindly add new claims 28-31, as follows:

28. (new) The pharmaceutical composition for prevention, treatment or therapy according to claim 10 wherein the pharmaceutical composition is suitable for intravenous administration.

29. (new) The pharmaceutical composition for prevention, treatment or therapy according to claim 10 wherein the pharmaceutical composition is suitable for a single intravenous infusion or for continuous intravenous administration.

30. (new) Pharmaceutical compositions for prevention, treatment or therapy of diseases of the nervous tissues or the spinal cord as obtained by the method according to claim 23.

31. (new) A method for screening novel brain cell-protective agents or nerve cell-protective agents comprising using ginsenoside Rb1 or its metabolites as a leading compound(s).